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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/084,471	05/22/98	MURPHY	DK

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EXAMINER	

ZITOMER, S	
ART UNIT	PAPER NUMBER

1655
DATE MAILED:

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/084,471

Applicant(s)

Murphy et al.

Examiner

Stephanie Zitomer

Group Art Unit
1655



☒ Responsive to communication(s) filed on Feb 4, 1900

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-60 is/are pending in the application.

Of the above, claim(s) 17-21, 23, 25, 27, 29, 31-37, 39-51, and 55-60 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-16, 22, 24, 26, 28, 30, 38, and 52-54 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been received.

☐ received in Application No. (Series Code/Serial Number) _____

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 2, 7

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election

1. Applicant's election of Invention I in Paper No. 4 filed October 1, 1999 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse 37 CAR 1.111(b). See also M.P.E.P. § 818.03(a).

Informalities

2. The disclosure is objected to because of the following informalities: The Sequence Listing paper copy and CRF have been approved and entered in the record. However, the sequences in the figures are lacking SEQ ID NOS:.

Appropriate correction is required.

Rejection under 35 USC 101: Nonstatutory subject matter

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 1-16, 22, 24, 26, 28, 30 and 38 are rejected under 35 U.S.C. 101 because they are drawn to nonstatutory subject matter. The recitations "A genomic DNA containing a BRCA2 gene", "A DNA comprising a BRCA2 coding sequence" and "A haplotype of a BRCA2 coding sequence" read on naturally occurring DNA. This rejection can be overcome by amending the claims to identify the DNA as "isolated" and/or "purified".

Rejection under 35 USC 112, first paragraph: Lack of proper written description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-16, 22, 24, 26, 28, 30 and 38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are interpreted as broadly drawn to any BRCA2 coding sequence having the recited nucleotides

at the recited positions. Thus, the claims are drawn to a large genus of BRCA2 sequences for which the application discloses only five species. Analysis of the written description for adequacy according to 35 USC 112, first paragraph, requires consideration of (a) the predictability of the art; (b) disclosure of complete or partial structure; (c) physical and chemical characteristics; (d) function coupled with known correlation between structure and function (Fed. Reg. 63 (114):32639-32645, June 15, 1998). With regard to (a), on a purely statistical basis the claimed BRCA2 coding sequence of approximately 10482 nucleotides, based on SEQ ID NO:4, minus the 71 defined nucleotide positions, multiplied by the 4 possible nucleotides and by the human population would have been predicted by one of skill in the art to have at least one previously unidentified nucleotide difference from the nucleotide sequences of the presumed reference sequences, BRCA2^(omi1-5). However, the nucleotide position of that at least one nucleotide difference would have been unpredictable in view of the lack of written description in the specification and in the prior art of a basis for prediction such as a "hot spot" in the BRCA2 coding sequence. Furthermore, the prior art suggests that the incidence of mutations in BRCA2 is low (Teng et al. 1996 Nature Genetics 13:241-244). With respect to (b), disclosure of the partial structure, i.e., the 71 defined nucleotides, does not provide a basis for predicting the nucleotides at the other 10411 positions in the coding sequence absent description in the specification of a nexus between the defined and undefined individual nucleotides in the claimed sequences. One of skill in the art would have reasonably expected the physical and chemical characteristics of the claimed BRCA2 coding sequences to be generally similar to those of the five disclosed sequences, i.e., being a polymer composed of the four nucleotides, A, T, C, and G, capable of forming a double stranded helix conformation with its complementary sequence for which the boiling point and disassociation temperatures were known. However, the skilled artisan would have known further that these characteristics were not predictive for the precise arrangement of the four nucleotides in the DNA polymer, i.e., the nucleotide sequence. Lastly, the correlation between the structure, i.e., the nucleotide sequence, and the coding function of the claimed BRCA2 coding sequence would have been generally known to one of skill in the art. However, the function of a different nucleotide sequence with respect to whether a nucleotide change was polymorphic or mutational would not have been known a

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priori and thus was unpredictable. In addition to enablement the first paragraph of 112 requires a "written description". As set forth by the Court in *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, the written description must convey to one of skill in the art "with reasonable clarity" that as of the filing date applicant was in possession of the claimed invention. While the claimed BRCA2 coding sequences are fully enabled with respect to how to identify and use them, they lack adequate written description for the previously stated reasons.

Rejections under 35 USC 112, second paragraph: Indefiniteness: Claims not examined

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-16, 24, 26, 28, 30, 38 and 52-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) The claims are indefinite and have not been examined with respect to the prior art because the exon positions and "coding sequence" positions are not identified in the claims or elsewhere in the disclosure. It is not possible to search a nucleotide sequence "containing a BRCA2 gene" having the limitations recited in the claims without knowing the nucleotide positions of the exons and the identity and nucleotide numbering of the "coding sequence". No positional relationship is provided in the disclosure for the exons 5, 15 and 16 recited in claims 1-8 because in the Sequence Listing each is a separate sequence with its own nucleotide numbering independent of the gene sequence nucleotide numbering and the exons presented in the figures have no nucleotides numbers. The recitation in the claims of a reference sequence may overcome this rejection.

(b) Claims 1-8 lack proper antecedent basis for the "wherein" phrases because it is unclear whether they refer to the BRCA2 gene or some other gene in the "genomic DNA".

(c) Claims 2-8 lack proper antecedent basis in claim 1 for "the coding sequence" in which the nucleotides at designated positions are located because claim 1 does not recite a "coding sequence".

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(d) Claims 9-16 lack proper antecedent basis in claim 9 for the recited nucleotide number positions because claim 9 does not recite a sequence having numbered nucleotide positions.

(e) Claims 10-16 are grammatically incorrect in the recitation, "the coding sequence nucleotides are as follows:". It is suggested to recite --the coding sequence comprises the following nucleotides:--.

(f) Claims 22, 24, 26, 28 and 30 are confusing because the antecedent basis of the recited SEQ ID NO: is unclear, i.e., whether it is "haplotype" or "BRCA^(omi#)". It is suggested to change the first word "A" to --The-- and to delete "of" and "as" or to insert --the-- before "BRCA2" and delete "as" depending on the intended meaning of the claim language.

(g) Claim 38 lacks proper antecedent basis in being drawn to a product and depending from a method claim. The claim further lacks proper antecedent basis in depending from a nonelected claim.

(h) Claim 38 lacks proper antecedent basis for "the codon pairs". It is suggested to insert --given-- before "codon".

(i) Claim 38 is confusing in being drawn to "A BRCA2 coding sequence" whereas the recitation of "codon pairs" for each of ten nucleotide positions clearly defines more than one different sequence. Furthermore, it is unclear whether all ten of the first recited codons at each position and all ten of the second codons recited at each position are contained in two sequences, respectively, or whether the claim is drawn to any BRCA2 coding sequence having any combination of the twenty recited codons.

(j) Claims 52-54 are indefinite in the recitation "any fragments thereof" because "fragments" is not defined in the claims or in the specification and it is not understood in the context of the claims in that it may consist of a single nucleotide. It is suggested to use functional language, e.g., --encoding a BRCA2 protein-- to define "fragments" as indicated in the first full paragraph at page 19 of the specification.

(k) Claims 52-54 are confusing in the recitation "to induce replication and/or integration in a host cell", (l) because "to induce" is a recited use and therefore does not

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define "suitable regulatory sequences" and (ii) because the antecedent of "replication" is unclear, i.e., the DNA sequence or the vector. It is suggested to change the former to --which induces-- and to clarify the antecedent basis of the latter by, e.g., changing "replication" to --expression-- if applicable to the intended meaning of the claim. See page 19 cited above.

Rejections under 35 U.S.C. 102(b)/103(a): Anticipation/inherent properties

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claim 1 and 9 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Futreal et al. (GB 2 307 477, May 28, 1997). Futreal et al. disclose a genomic DNA containing a BRCA2 gene which includes the coding sequence (page 42, lines 35-38; page 43, lines 2-7; page 49, line 21). This rejection is based on judicial precedent following *In re Fitzgerald*, 205 USPQ 594 because EP '477 is silent with regard to the presence of the recited nucleotide sequences in the BRCA2 gene. However, the sequences recited in claims 1 and 9 are deemed to be inherent in the genomic BRCA2 gene of the reference because applicant states in the specification (pages 26-27) that the nucleotide sequences recited in claims 1 and 9 represent a correction of the published BRCA2 sequence, GenBank U43746. Therefore, one of skill in the art would have known that the genomic BRCA2 source of the GenBank sequence contained the recited sequences and that the reference BRCA2 gene contained the recited sequences because correction of a previously identified sequence does not alter the natural sequence in genomic BRCA2. The burden is on applicant to show that the claimed BRCA2 is either different or nonobvious over that of Futreal et al..

7. Claim 1 and 9 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Tavtigian et al. Nature Genetics 12, March, 1996). Tavtigian et al. disclose a genomic DNA containing a BRCA2 gene which includes the coding sequence (page 333, column 2, line 1; page 333, second full paragraph at column 2; page 337, second full paragraph at column 2). This rejection is based on

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judicial precedent following *In re Fitzgerald*, 205 USPQ 594 because Tavgigian et al. is silent with regard to the presence of the recited nucleotide sequences in the BRCA2 gene. However, the sequences recited in claims 1 and 9 are deemed to be inherent in the genomic BRCA2 gene of the reference because applicant states in the specification (pages 26-27) that the nucleotide sequences recited in claims 1 and 9 represent a correction of the published BRCA2 sequences, GenBank U43746 and BIC. Therefore, one of skill in the art would have known that the genomic BRCA2 sources of the GenBank and BIC sequences contained the recited sequences and that the reference BRCA2 gene contained the recited sequences because correction of a previously identified sequence does not alter the natural sequence in genomic BRCA2. The burden is on applicant to show that the claimed BRCA2 is either different or nonobvious over that of Futreal et al..

Conclusion

8. **No claim is allowed.**

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie Zitomer whose telephone number is (703) 308-3985. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152. The official fax phone number for this Group is (703) 308-4242. The unofficial fax number is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SE Zitomer

Stephanie Zitomer, Ph.D.

March 6, 2000

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